SUPPLEMENTARY MATERIALS

Table S1. Complete list of input parameters, their distributions and data source

Model parameter	Base case	Range (one-way sensitivity analysis)	Data source
Cost			
Dabigatran (brand name), monthly	296.23	NA	(1, 2)
Dabigatran (generic), monthly	257.72	(62.21-257.72)	(1-3)
Aspirin, monthly	0.64	(0.16-6.42)	(4)
Event cost of minor stroke	19639.40	(17453-21816.84)	(5)
Monthly cost of minor stroke	840.05	(219.05-1461.05)	(5)
Event cost of major stroke	31045.69	(27588.36-34503.02)	(5)
Monthly cost of major stroke	1327.75	(345.11-2309.36)	(5)
Event cost of RIND event	11802.03	(10488.74-13117.39)	(5)
Event cost of ICH	47790.90	(34252.97-61330.89)	(5)
Monthly cost of ICH	3099.82	(162.22-6036.38)	(5)
Monthly cost of stroke and ICH	3935.73	(206.65-7665.84)	(5)
Event cost of ECH	15658.20	(13300.28-18015.1)	(5)
Event cost of minor bleeding	44.43	(0-216.99)	(4)
Event cost of MI	34368.69	(30831.80-37906.62)	(5)
Monthly cost of MI	586.90	(551.77-1930.15)	(5)
Event cost of nonevent death	6469.32	(3796.24-8134.95)	(4)
Utility			
Healthy on dabigatran (Annual)	0.994	(0.975-1)	(6)
Healthy on aspirin (Annual)	0.998	(0.994-1)	(7)
Disutility of major neurologic event (Annual)	-0.61	(-1-0)	(7)
Disutility of minor neurologic event (Annual)	-0.24	(-1-0)	(7)
Disutility of Non-ICH bleed event (Annual)	-0.16	(-0.3-0)	(8)
Disutility of MI (Annual)	-0.16	(-0.3-0)	(9)
Transition Probabilities			
Baseline rate of minor bleeding on warfarin for patients in low bleed risk category (%/year)	8.089	---	(10)

Baseline rate of minor bleeding on warfarin for patients in medium bleed risk category (%/year)	10.091	---	(10)
Baseline rate of minor bleeding on warfarin for patients in high bleed risk category (%/year)	14.452	---	(10)
Hazard ratio of minor bleeding comparing brand dabigatran to warfarin	0.91	(0.85-0.97)	(11)
Relative risk of minor bleeding comparing aspirin to warfarin	0.63	(0.32-1.22)	(12)
Baseline rate of stroke on warfarin for patients in low stroke risk category (%/year)	0.949	---	IBM
Baseline rate of stroke on warfarin for patients in medium stroke risk category (%/year)	1.424	---	IBM
Baseline rate of stroke on warfarin for patients in high stroke risk category (%/year)	2.555	---	IBM
Hazard ratio of stroke comparing brand dabigatran to warfarin	0.76	(0.6-0.98)	(11)
Relative risk of stroke comparing aspirin to warfarin	2.08	(1.59-2.7)	(13)
Proportion of fatal ischemic stroke with dabigatran (%)	8.2	(8.2-10.1)	(4, 14-17)
Proportion of major ischemic stroke with dabigatran (%)	40.2	(40.2-41.7)	
Proportion of minor ischemic stroke with dabigatran (%)	42.5	(34.8-42.5)	
Proportion of ischemic stroke with no residual deficit with dabigatran (%)	9.1	(9.1-13.3)	
Proportion of fatal ischemic stroke with aspirin (%)	17.9	(10.1-17.9)	(4, 14-16)
Proportion of major ischemic	30	(30-41.1)	

stroke with aspirin (%)			
Proportion of minor ischemic stroke with aspirin (%)	41	(34.8-41)	
Proportion of ischemic stroke with no residual deficit with aspirin (%)	11	(11-13.3)	
Relative risk of stoke per 10 years of life	1.4	---	(18)
Baseline rate of ICH on warfarin for patients in low bleed risk category (%/year)	0.497	---	IBM, (10)
Baseline rate of ICH on warfarin for patients in medium bleed risk category (%/year)	0.620	---	
Baseline rate of ICH on warfarin for patients in high bleed risk category (%/year)	0.887	---	
Relative risk of ICH per 10 years of life	1.97	---	(18)
Relative risk of ICH comparing aspirin to warfarin	0.51	(0.16-1.6)	(12)
Proportion of fatal ICH with dabigatran or aspirin (%)	36.4	(28.3-45.2)	(19)
Proportion of major ICH with dabigatran or aspirin (%)	14.1	(9-21.4)	
Proportion of minor ICH with dabigatran or aspirin (%)	49.5	---	
Hazard ratio of ICH comparing brand dabigatran to warfarin	0.4	(0.27-0.6)	(11)
Baseline rate of ECH on warfarin for patients in low bleed risk category (%/year)	1.916	---	IBM, (10)
Baseline rate of ECH on warfarin for patients in medium bleed risk category (%/year)	2.390	---	
Baseline rate of ECH on warfarin for patients in high bleed risk category (%/year)	3.423	---	

Hazard ratio of ECH comparing brand dabigatran to warfarin	1.07	(0.78-1.25)	(11)
Relative risk of ECH comparing aspirin to warfarin	1.14	(0.47-2.73)	(12)
Proportion of fatal ECH (%)	1.47	(1-4)	(4)
Baseline rate of MI on warfarin (%/year)	1.12	(0.93-1.31)	(10)
Relative risk of MI per 10 years of life	1.3	---	(4, 14, 15, 17)
Hazard ratio of MI comparing brand dabigatran to warfarin	1.31	(0.89-1.91)	(11)
Relative risk of MI comparing aspirin to warfarin	1.42	(0.84-2.39)	(12)
Proportion of fatal MI (%)	16.6	(15.8-17.4)	(4)
Relative risk of nonevent death with nonvalvular atrial fibrillation	1.3	(1.12-1.62)	(20)
Relative risk of nonevent death with nonvalvular atrial fibrillation and stroke	2.3	(1.3-3)	(21)
Abbreviations: RIND=reversible ischemic neurological damage; ICH=intracranial hemorrhage; ECH=extracranial hemorrhage; MI= Myocardial Infarction			

Table S2. The calculation of state and transition utilities

Health state	Calculations of state utilities (monthly utilities)
Well with AF	0.994/12 = 0.08283
RIND	0.994/12 = 0.08283
Minor stroke	0.994/12-0.24/12 = 0.06283
Major stroke	0.994/12-0.61/12 = 0.032
Minor ICH	0.998/12-0.24/12 = 0.06317
Major ICH	0.998/12-0.61/12 = 0.03233
Minor stroke on aspirin	0.998/12-0.24/12 = 0.06317
Major stroke on aspirin	0.998/12-0.61/12 = 0.03233
Stroke and ICH	0.998/12-0.61/12 = 0.03233

MI	0.994/12 = 0.08283
ECH	0.998/12 = 0.08317
Death	0
Transition event	**Calculations of transition utilities (QALY)**
RIND	-0.24
MI	-0.16*(30/365.25) = -0.013141
ECH	-0.16*(14/365.25) = -0.006133
Minor bleed	-0.16*(2/365.25) = -0.000876
Abbreviations: AF=atrial fibrillation; RIND=reversible ischemic neurological damage; ICH=intracranial hemorrhage; ECH=extracranial hemorrhage; MI= Myocardial Infarction; QALY=quality-adjusted life year	

Detailed Calculation of Transition Probabilities (Event Rate)

Stroke

The ischemic stroke rates for patients on warfarin at each CHA_2DS_2-VASc score category were derived from IBM MarketScan[®] Databases. Stroke rates stratified by CHA_2DS_2-VASc score category for those receiving brand dabigatran were derived by multiplying the on-warfarin rates by the HR of ischemic stroke on dabigatran reported in RE-LY trial. Stroke rates for those on generic dabigatran were derived by multiplying the on-dabigatran (brand) rates by the HR of stroke comparing brand and generic dabigatran obtained from the PK/PD model.

Bleeding events

The overall (without stratification by HAS-BLED score) bleeding rates (minor bleeding, ICH and ECH) on warfarin were obtained from an existing clinical trial. Bleeding rates (minor bleeding, ICH and ECH) stratified by HAS-BLED score for those on warfarin were derived by multiplying the overall bleeding rates by the relative risks for bleeding overall and between each HAS-BLED score category. These relative risks were obtained from IBM MarketScan[®] Databases. The IBM MarketScan Database Analysis section describes in detail how the relative risks were estimated. The bleeding rates stratified by the HAS-BLED score for those on dabigatran were

derived by multiplying the on-warfarin bleeding rates stratified by HAS-BLED score by the hazard ratios of bleeding for dabigatran versus warfarin obtained from the RELY clinical trial.(11) The bleeding rates for those on generic dabigatran were derived by multiplying the on-dabigatran (brand) bleeding rates stratified by HAS-BLED score by the hazard ratio of bleeding comparing generic to brand dabigatran obtained from the PK/PD model.

Myocardial infarction

On-warfarin myocardial infarction rate was obtained from clinical trial. Myocardial infarction rate for those on (brand) dabigatran was calculated by multiplying the on-warfarin rate by the hazard ratio of MI comparing warfarin to dabigatran. The myocardial infarction rate for those on generic dabigatran was calculated by multiplying the on-dabigatran (brand) rate by the hazard ratio of MI comparing generic to brand. This hazard ratio was based on the difference in hazard ratio of MI between 150 mg dabigatran versus control treatment and 110 mg dabigatran versus control treatment obtained from meta-analysis, assuming a linear relationship between dabigatran dose and MI.

IBM MarketScan® Database Analysis

This section describes the analysis we conducted in IBM MarketScan® database to obtain the parameters described in the Transition Probability section. Use of MarketScan data for this study were considered exempt from review by the University of Florida Institutional Review Board.

All new users of warfarin from Oct 19, 2010 to June 30, 2015 were selected based on the national drug code (NDC). The index date is defined as the date of the first prescription. Patients were required to have one inpatient or two outpatient diagnosis of Atrial Fibrillation (AF) within 60 days before the index date and at least 12

months of continuous enrollment in the health plan before the index date. Patients with diagnosis of mitral valve disease, heart valve repair or replacement, or joint replacement during the pre-index period were excluded.

All patients were grouped into three categories based on the estimated CHA_2DS_2-VASc score (Low stroke risk: 2-3; Medium stroke risk: 4; High stroke risk: >=5). Patients in each subgroup were followed until the occurrence of ischemic stroke (ICD-9-CM diagnosis code, 433.x1, 434.x1 and 436) or transient ischemic attack (ICD-9-CM diagnosis code, 435.x). The stroke rates stratified by CHA_2DS_2-VASc score category were calculated:

$$Stroke\ rate = \frac{Number\ of\ event\ (ischemic\ stroke\ or\ transient\ ischemic\ attack)}{Total\ follow\ up\ person\text{-}time\ (person\text{-}year)}$$

All the bleeding rates (minor bleeding, ICH and ECH) were calculated using the same set of relative risks between overall and each HAS-BLED score category. Patients were group into three categories based on estimated HAS-BLED score (Low bleed risk: 0-1; Medium: 2; High: >=3). Patients were followed until the occurrence of moderate or minor bleeding events. Moderate bleeding was defined as bleeding events in inpatient or emergency department that did not meet the criteria for major bleeding (occurrence at critical sites, transfusions needed and death). Minor bleeding was defined as bleeding events treated in an outpatient setting. The overall moderate/ minor bleeding rate and bleeding rate for each bleed risk subgroup were calculated:

$$Bleeding\ rate = \frac{Number\ of\ event\ (moderate\ or\ minor\ bleeding\ event)}{Total\ follow\ up\ person\text{-}time\ (person\text{-}year)}$$

The relative risks of bleeding between overall population and each individual bleed

risk category were then calculated.

Patients were grouped into nine subgroups based on stroke and bleeding risk

categories described earlier. Their mean age at index date and standard deviation
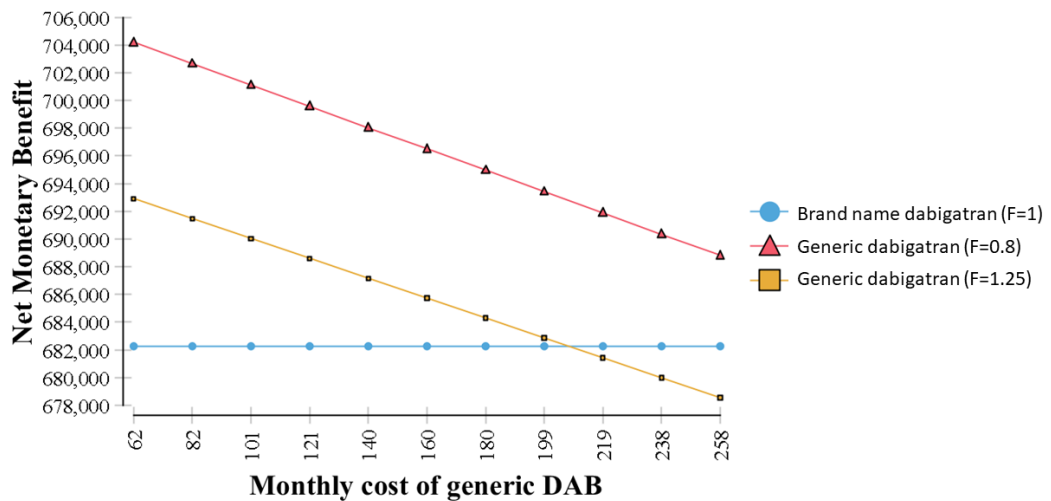
were calculated.

Figure S1-S4 shows the result of one-way sensitivity analysis comparing brand dabigatran and extreme cases of generic dabigatran.
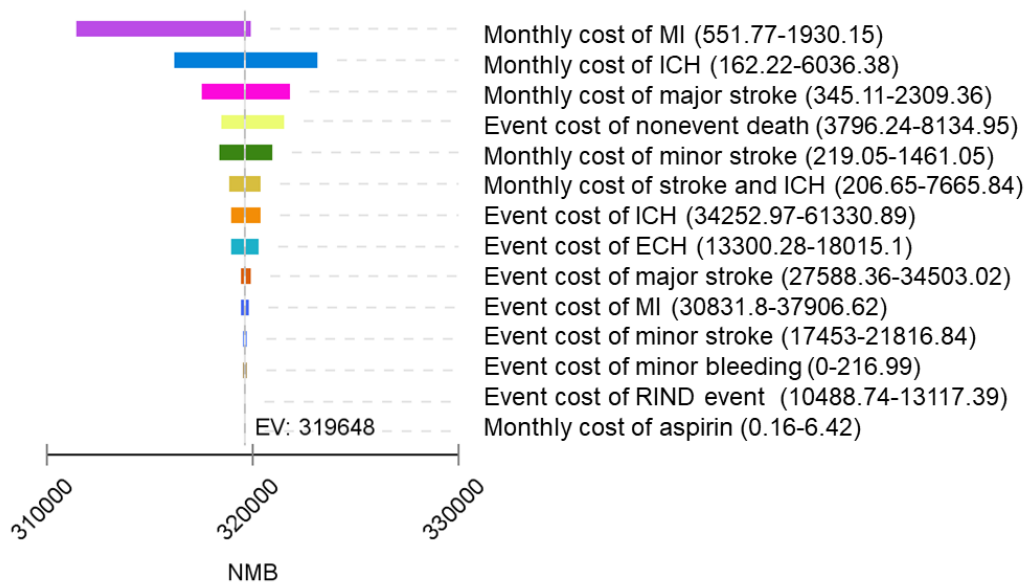
Sensitivity Analysis (WTP=50,000)

A)
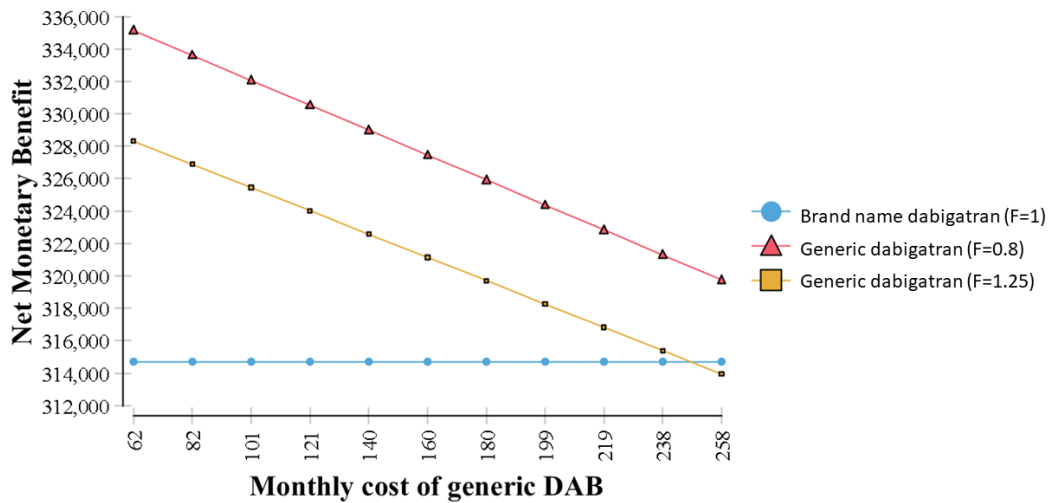
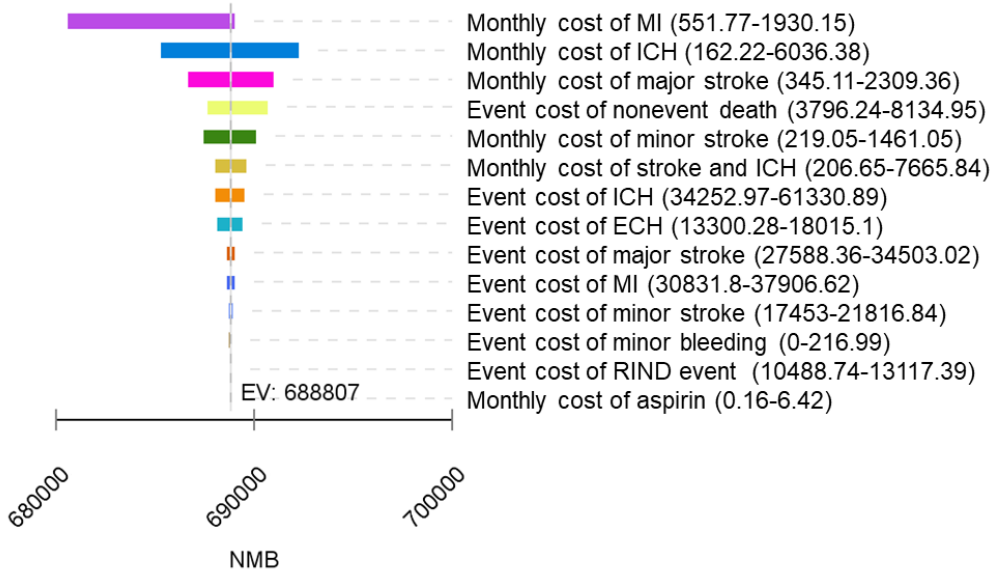### Sensitivity Analysis (WTP=100,000)

B)

Figure S1. net monetary benefit of brand and extreme cases of generic dabigatran at varying generic dabigatran cost A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.

Tornado Diagram – Net Monetary Benefits (WTP=50,000)

- Monthly cost of MI (551.77-1930.15)
- Monthly cost of ICH (162.22-6036.38)
- Monthly cost of major stroke (345.11-2309.36)
- Event cost of nonevent death (3796.24-8134.95)
- Monthly cost of minor stroke (219.05-1461.05)
- Monthly cost of stroke and ICH (206.65-7665.84)
- Event cost of ICH (34252.97-61330.89)
- Event cost of ECH (13300.28-18015.1)
- Event cost of major stroke (27588.36-34503.02)
- Event cost of MI (30831.8-37906.62)
- Event cost of minor stroke (17453-21816.84)
- Event cost of minor bleeding (0-216.99)
- Event cost of RIND event (10488.74-13117.39)
- Monthly cost of aspirin (0.16-6.42)

EV: 319648

NMB

Tornado Diagram – Net Monetary Benefits (WTP=100,000)

- Monthly cost of MI (551.77-1930.15)
- Monthly cost of ICH (162.22-6036.38)
- Monthly cost of major stroke (345.11-2309.36)
- Event cost of nonevent death (3796.24-8134.95)
- Monthly cost of minor stroke (219.05-1461.05)
- Monthly cost of stroke and ICH (206.65-7665.84)
- Event cost of ICH (34252.97-61330.89)
- Event cost of ECH (13300.28-18015.1)
- Event cost of major stroke (27588.36-34503.02)
- Event cost of MI (30831.8-37906.62)
- Event cost of minor stroke (17453-21816.84)
- Event cost of minor bleeding (0-216.99)
- Event cost of RIND event (10488.74-13117.39)
- Monthly cost of aspirin (0.16-6.42)

EV: 688807

NMB

A)

Figure S2. Tornado diagram of net monetary benefit at varying event and monthly cost comparing brand and extreme cases of generic dabigatran A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.

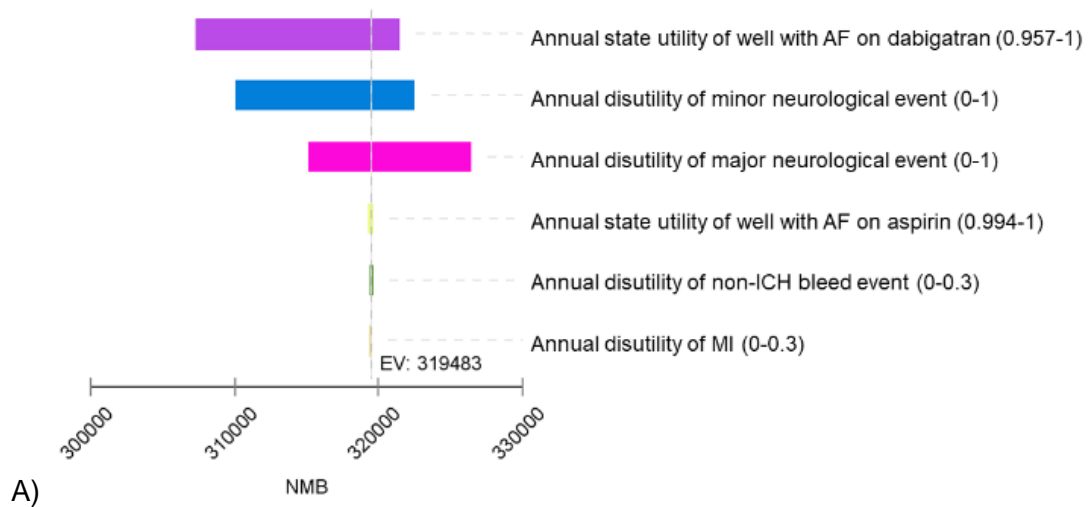**Tornado Diagram – Net Monetary Benefits (WTP=50,000)**

A)

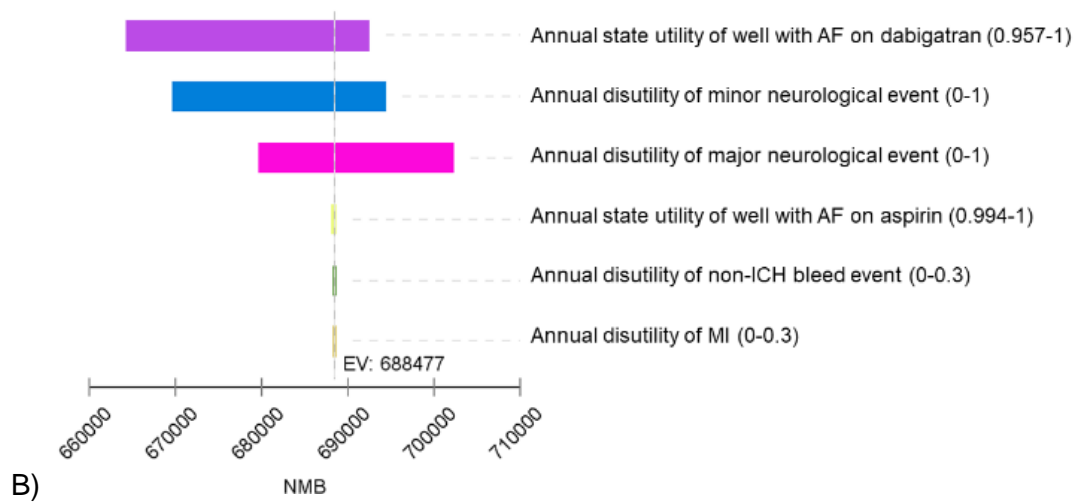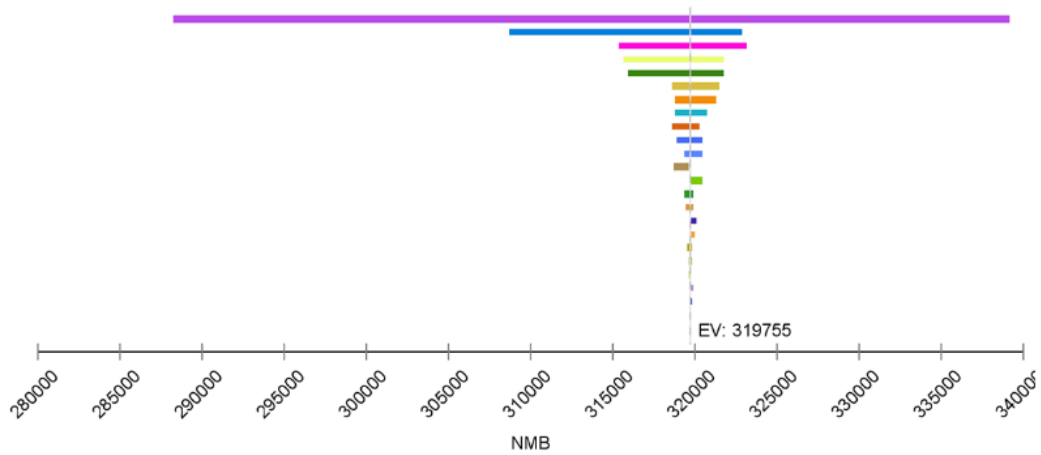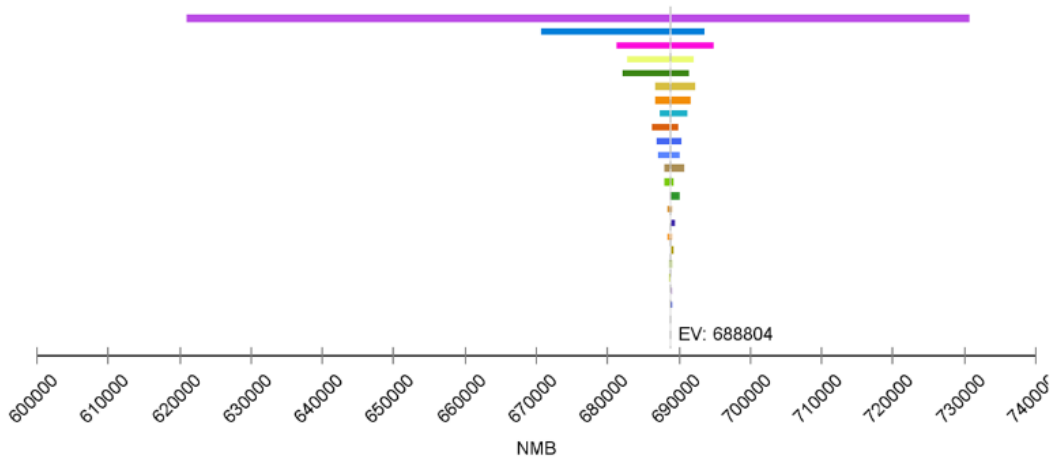**Tornado Diagram – Net Monetary Benefits (WTP=100,000)**

B)

Figure S3. Tornado diagram of net monetary benefit at varying utilities comparing brand and extreme cases of generic dabigatran A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.

Tornado Diagram- Net Monetary Benefits

(WTP=50,000)

EV: 319755

NMB

■ RR of nonevent death with nonvalvular AF (1.12-1.61)
■ HR of ICH comparing brand dabigatran to warfarin (0.27-0.6)
■ HR of stroke comparing brand dabigatran to warfarin (0.6-0.98)
■ HR of MI comparing dabigatran to warfarin (0.89-1.91)
■ RR of ICH comparing aspirin to warfarin (0.16-1.6)
■ RR of stroke comparing aspirin to warfarin (1.59-2.7)
■ Baseline rate of MI on warfarin (0.0093-0.0131)
■ RR of MI comparing aspirin to warfarin (0.84-2.39)
■ Proportion of fatal ECH (0.01-0.04)
■ HR of ECH comparing brand dabigatran to warfarin (0.78-1.25)
■ RR of ECH comparing aspirin to warfarin (0.47-2.73)
■ RR of nonevent death AF and stroke (1.3-3)
■ Proportion of ischemic stroke with no residual deficit with dabigatran (0.091-0.133)
■ Proportion of fatal MI (0.158-0.174)
■ Proportion of major ICH (0.09-0.214)
■ Proportion of ischemic stroke with no residual deficit with aspirin (0.11-0.133)
■ Proportion of fatal ischemic stroke with aspirin (0.101-0.179)
■ Proportion of fatal ICH with dabigatran or aspirin (0.283-0.452)
■ Proportion of major ischemic stroke with aspirin (0.3-0.411)
■ Proportion of minor ischemic stroke with dabigatran (0.09-0.214)
■ Proportion of fatal ischemic stroke with dabigatran (0.082-0.101)
■ Proportion of minor ischemic stroke with aspirin (0.348-0.41)
■ Proportion of major ischemic stroke with dabigatran (0.402-0.417)
■ RR of minor bleeding comparing aspirin to warfarin (0.32-1.22)
■ HR of minor bleeding comparing dabigatran to warfarin (0.85-0.97)

A)

Tornado Diagram- Net Monetary Benefits
(WTP=100,000)

EV: 688804

NMB

RR of nonevent death with nonvalvular AF (1.12-1.61)
HR of ICH comparing brand dabigatran to warfarin (0.27-0.6)
HR of stroke comparing brand dabigatran to warfarin (0.6-0.98)
RR of ICH comparing aspirin to warfarin (0.16-1.6)
HR of MI comparing dabigatran to warfarin (0.89-1.91)
RR of stroke comparing aspirin to warfarin (1.59-2.7)
RR of nonevent death AF and stroke (1.3-3)
Baseline rate of MI on warfarin (0.0093-0.0131)
RR of MI comparing aspirin to warfarin (0.84-2.39)
Proportion of fatal ECH (0.01-0.04)
HR of ECH comparing brand dabigatran to warfarin (0.78-1.25)
RR of ECH comparing aspirin to warfarin (0.47-2.73)
Proportion of fatal MI (0.158-0.174)
Proportion of ischemic stroke with no residual deficit with dabigatran (0.091-0.133)
Proportion of major ICH (0.09-0.214)
Proportion of ischemic stroke with no residual deficit with aspirin (0.11-0.133)
Proportion of fatal ICH with dabigatran or aspirin (0.283-0.452)
Proportion of fatal ischemic stroke with aspirin (0.101-0.179)
Proportion of major ischemic stroke with aspirin (0.3-0.411)
Proportion of minor ischemic stroke with dabigatran (0.09-0.214)
Proportion of fatal ischemic stroke with dabigatran (0.082-0.101)
Proportion of minor ischemic stroke with aspirin (0.348-0.41)
Proportion of major ischemic stroke with dabigatran (0.402-0.417)
RR of minor bleeding comparing aspirin to warfarin (0.32-1.22)
HR of minor bleeding comparing dabigatran to warfarin (0.85-0.97)

B)

Figure S4. Tornado diagram of net monetary benefit at varying transition probabilities comparing brand and extreme cases of generic dabigatran A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.

Figure S5-S7 shows the result of one-way sensitivity analysis comparing brand

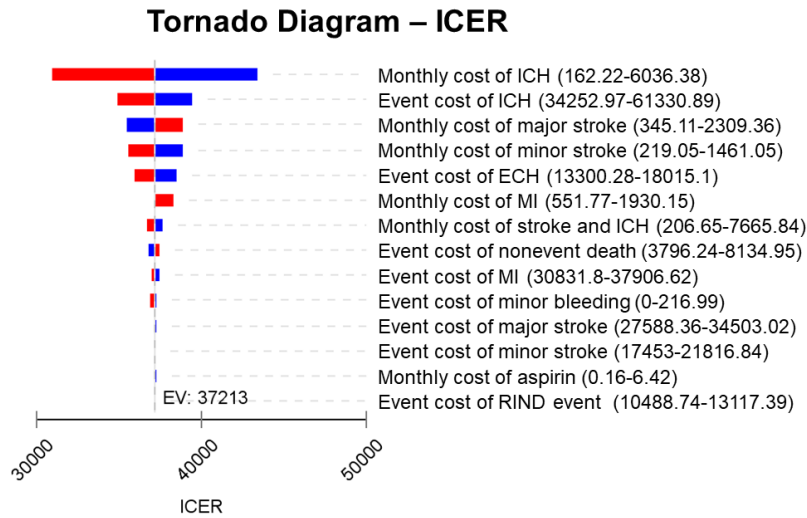dabigatran to F=1.25 generic dabigatran.

Tornado Diagram – ICER

Monthly cost of ICH (162.22-6036.38)
Event cost of ICH (34252.97-61330.89)
Monthly cost of major stroke (345.11-2309.36)
Monthly cost of minor stroke (219.05-1461.05)
Event cost of ECH (13300.28-18015.1)
Monthly cost of MI (551.77-1930.15)
Monthly cost of stroke and ICH (206.65-7665.84)
Event cost of nonevent death (3796.24-8134.95)
Event cost of MI (30831.8-37906.62)
Event cost of minor bleeding (0-216.99)
Event cost of major stroke (27588.36-34503.02)
Event cost of minor stroke (17453-21816.84)
Monthly cost of aspirin (0.16-6.42)
Event cost of RIND event (10488.74-13117.39)

EV: 37213

Figure S5. Tornado diagram of incremental cost-effectiveness ratio comparing brand

and F=1.25 generic dabigatran at varying event and monthly.

Tornado Diagram – ICER

Annual disutility of minor neurological event (0-1)

Annual state utility of well with AF on dabigatran (0.957-1)

Annual disutility of major neurological event (0-1)

Annual state utility of well with AF on aspirin (0.994-1)

Annual disutility of non-ICH bleed event (0-0.3)
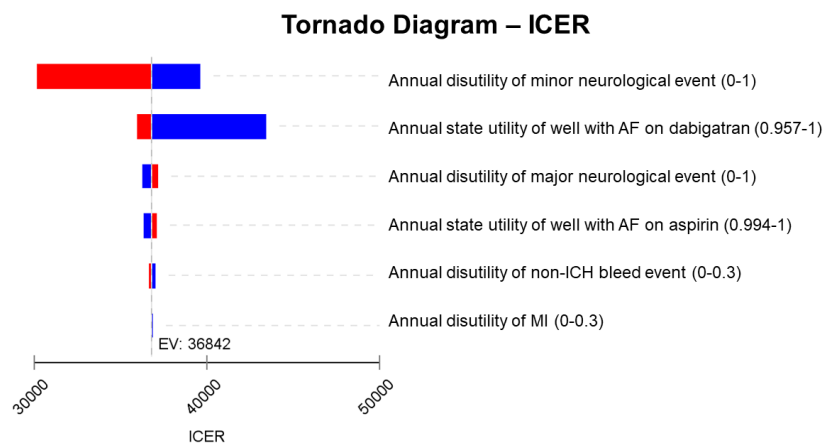
Annual disutility of MI (0-0.3)

EV: 36842

Figure S6. Tornado diagram of incremental cost-effectiveness ratio comparing brand

and F=1.25 generic dabigatran at varying utilities.

Tornado Diagram- ICER

HR of ECH comparing
dabigatran to warfarin (0.78-1.25)

Baseline rate of MI on
warfarin (0.0093-0.0131)

HR of MI comparing
dabigatran to warfarin (0.89-1.91)

HR of ICH comparing
dabigatran to warfarin (0.27-0.85)
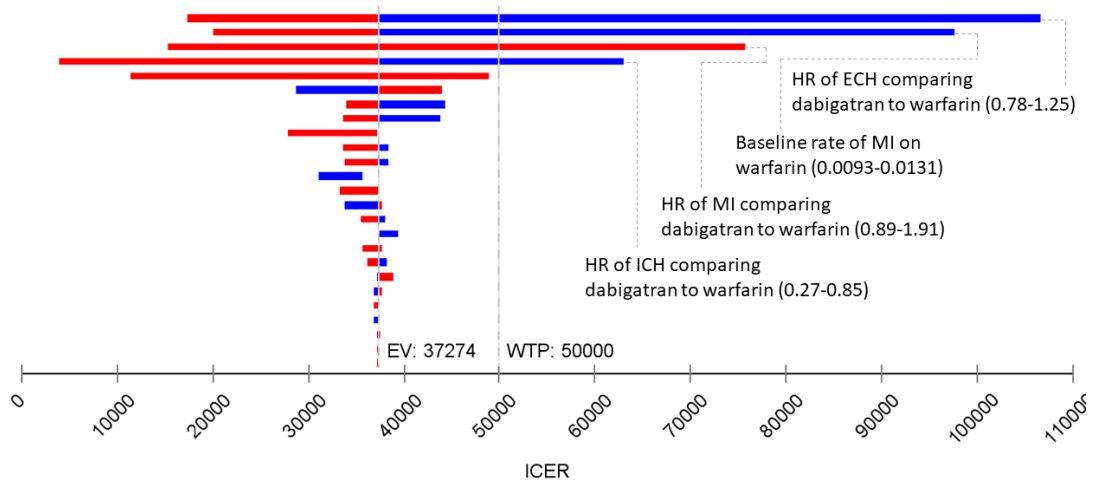
EV: 37274   WTP: 50000

ICER

Figure S7. Tornado diagram of incremental cost-effectiveness ratio comparing brand

and F=1.25 generic dabigatran at varying transition probabilities.

Figure S8-S11 shows the result of one-way sensitivity analysis comparing

brand dabigatran and less extreme cases of generic dabigatran.
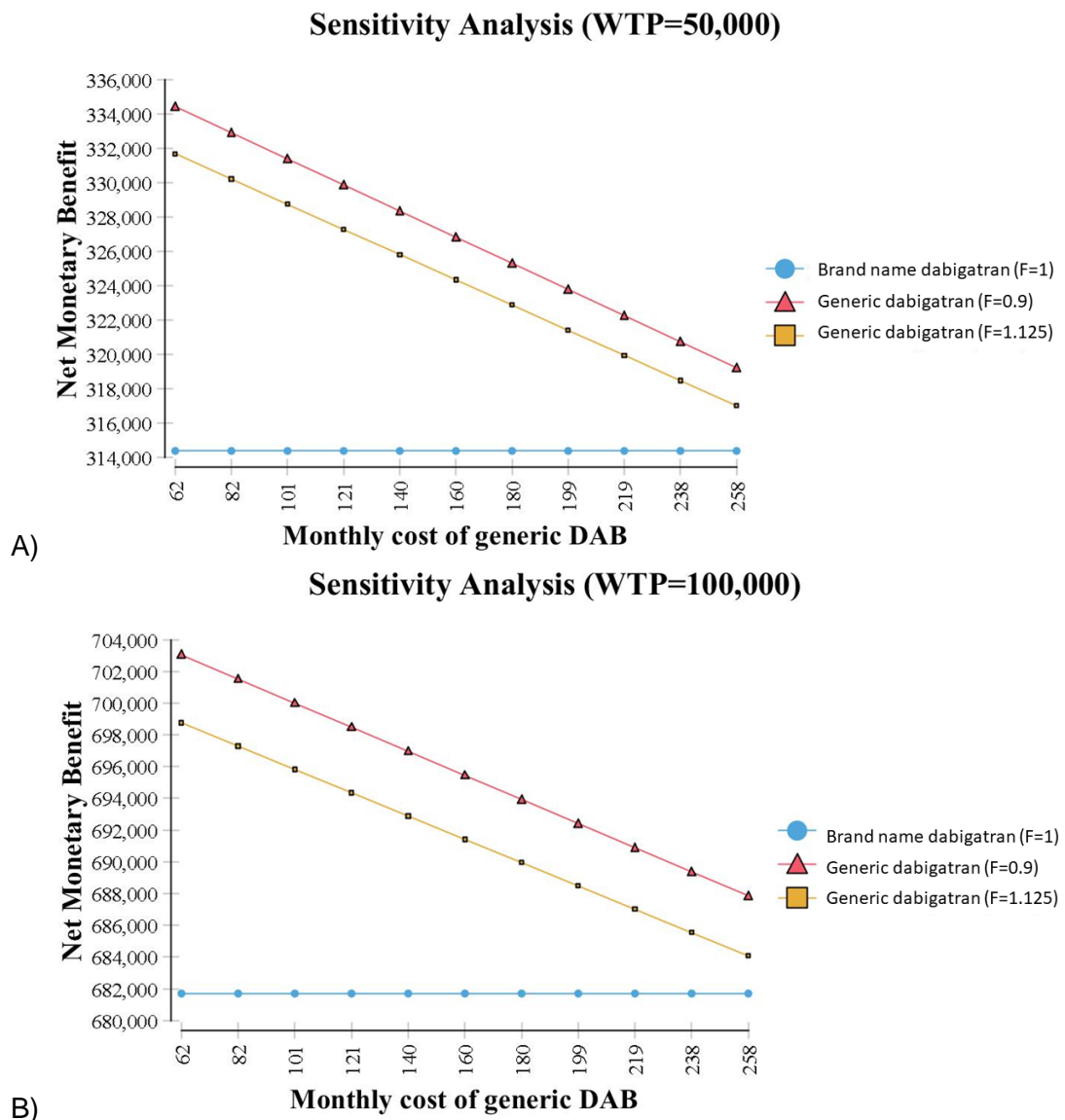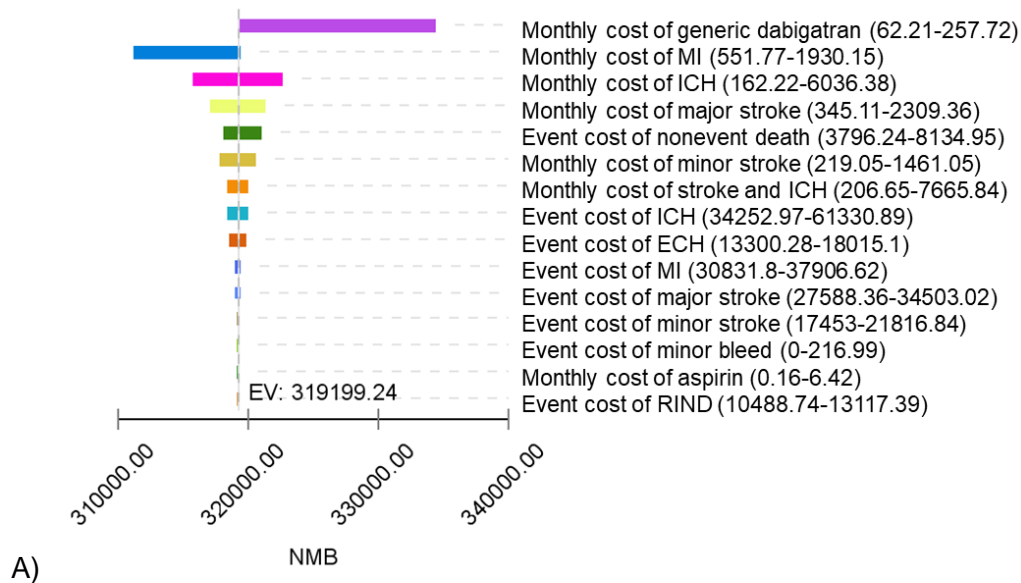

A)

B)

Figure S8. Net monetary benefit of brand and less extreme cases of generic

dabigatran at varying generic dabigatran cost A) using willingness-to-pay threshold of

50,000 B) using willingness-to-pay threshold of 100,000.

Tornado Diagram – Net Monetary Benefit (WTP=50,000)

Monthly cost of generic dabigatran (62.21-257.72)
Monthly cost of MI (551.77-1930.15)
Monthly cost of ICH (162.22-6036.38)
Monthly cost of major stroke (345.11-2309.36)
Event cost of nonevent death (3796.24-8134.95)
Monthly cost of minor stroke (219.05-1461.05)
Monthly cost of stroke and ICH (206.65-7665.84)
Event cost of ICH (34252.97-61330.89)
Event cost of ECH (13300.28-18015.1)
Event cost of MI (30831.8-37906.62)
Event cost of major stroke (27588.36-34503.02)
Event cost of minor stroke (17453-21816.84)
Event cost of minor bleed (0-216.99)
Monthly cost of aspirin (0.16-6.42)
Event cost of RIND (10488.74-13117.39)

EV: 319199.24

310000.00 320000.00 330000.00 340000.00

NMB

A)

Tornado Diagram – Net Monetary Benefit (WTP=100,000)

Monthly cost of generic dabigatran (62.21-257.72)
Monthly cost of MI (551.77-1930.15)
Monthly cost of ICH (162.22-6036.38)
Monthly cost of major stroke (345.11-2309.36)
Event cost of nonevent death (3796.24-8134.95)
Monthly cost of minor stroke (219.05-1461.05)
Monthly cost of stroke and ICH (206.65-7665.84)
Event cost of ICH (34252.97-61330.89)
Event cost of ECH (13300.28-18015.1)
Event cost of MI (30831.8-37906.62)
Event cost of major stroke (27588.36-34503.02)
Event cost of minor stroke (17453-21816.84)
Event cost of minor bleed (0-216.99)
Monthly cost of aspirin (0.16-6.42)
Event cost of RIND (10488.74-13117.39)

EV: 687841.57

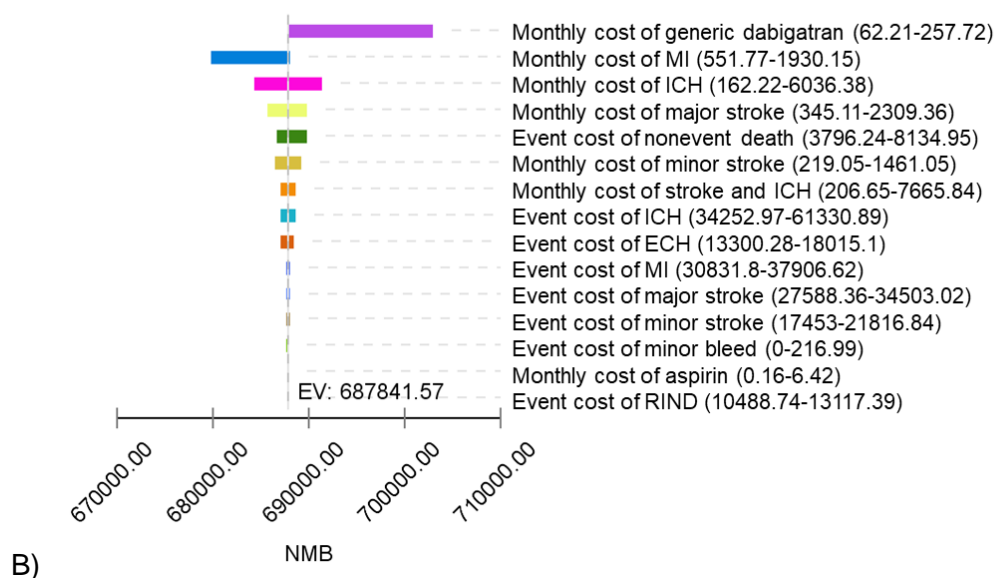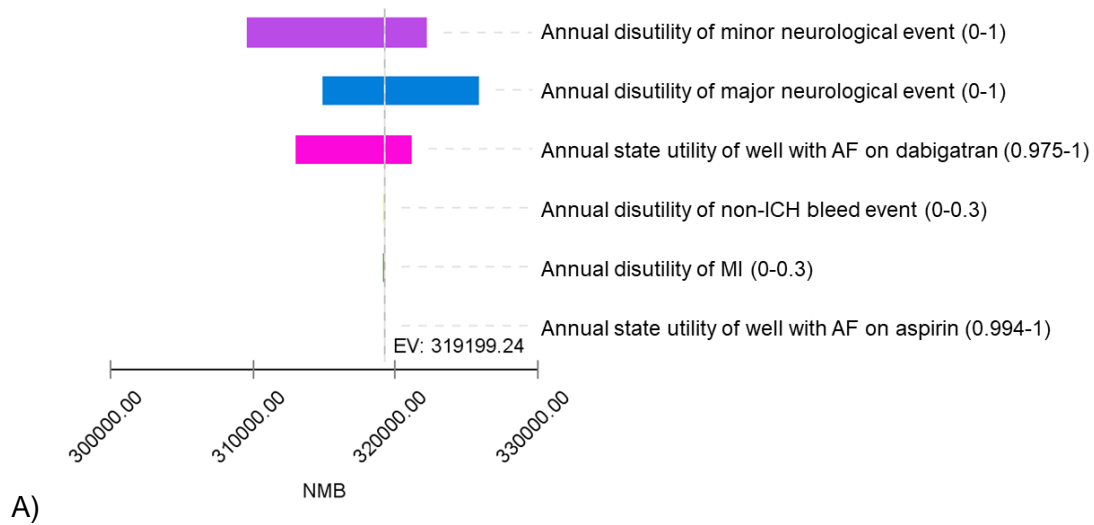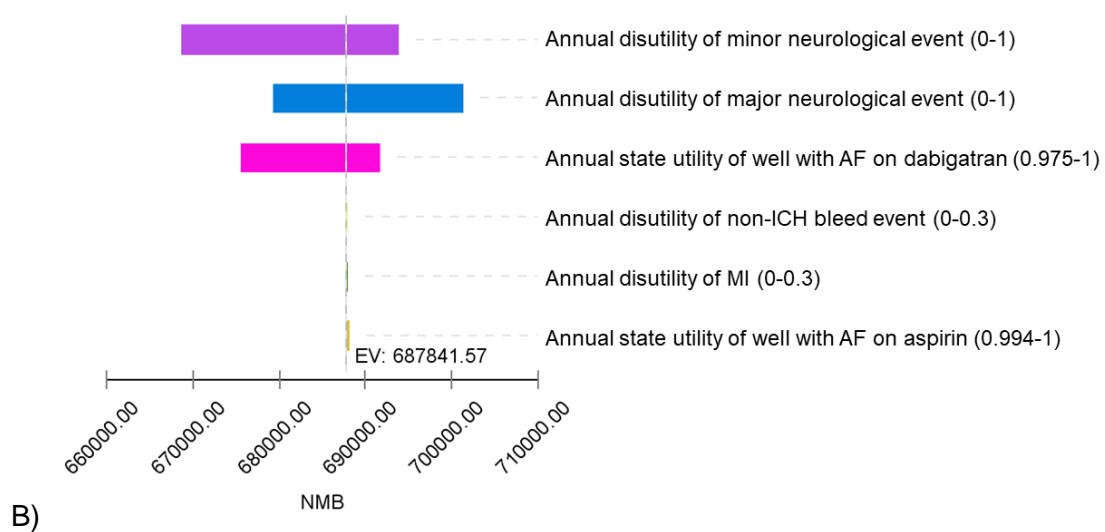670000.00 680000.00 690000.00 700000.00 710000.00

NMB

B)

Figure S9. Tornado diagram of Net monetary benefit comparing brand and less extreme cases of generic dabigatran at varying event and monthly cost A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.

Tornado Diagram – Net Monetary Benefit

(WTP=50,000)

Annual disutility of minor neurological event (0-1)

Annual disutility of major neurological event (0-1)

Annual state utility of well with AF on dabigatran (0.975-1)

Annual disutility of non-ICH bleed event (0-0.3)

Annual disutility of MI (0-0.3)

Annual state utility of well with AF on aspirin (0.994-1)

EV: 319199.24

300000.00   310000.00   320000.00   330000.00

NMB

A)

Tornado Diagram – Net Monetary Benefit

(WTP=100,000)

Annual disutility of minor neurological event (0-1)

Annual disutility of major neurological event (0-1)

Annual state utility of well with AF on dabigatran (0.975-1)

Annual disutility of non-ICH bleed event (0-0.3)

Annual disutility of MI (0-0.3)

Annual state utility of well with AF on aspirin (0.994-1)

EV: 687841.57

660000.00   670000.00   680000.00   690000.00   700000.00   710000.00

NMB

B)

Figure S10. Tornado diagram of net monetary benefit comparing brand and less extreme cases of generic dabigatran at varying utilities A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.
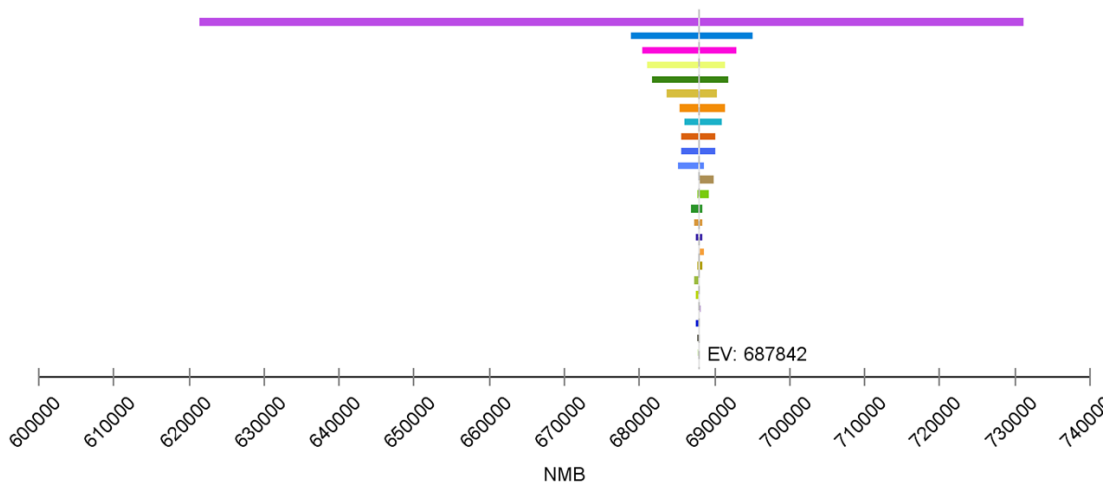
Tornado Diagram – Net Monetary Benefit

(WTP=50,000)

EV: 319199

NMB
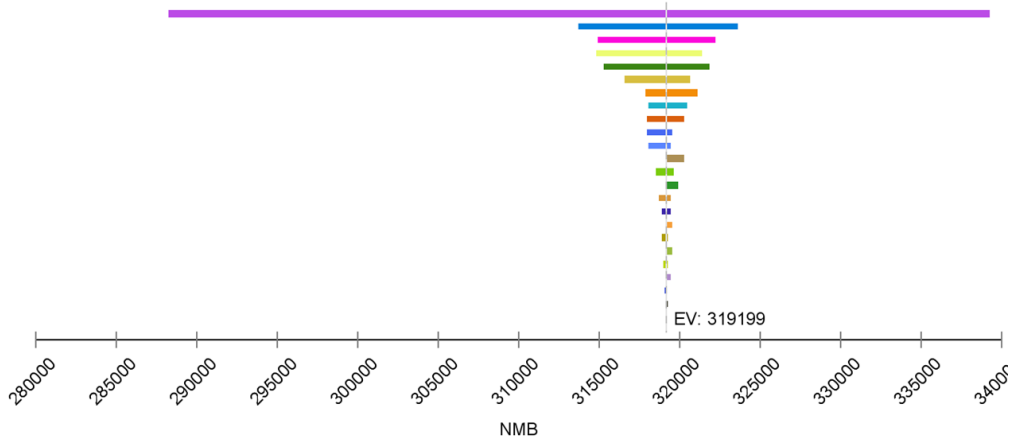
■ RR of nonevent death with nonvalvular AF (1.12-1.61)
■ HR of ICH comparing brand dabigatran to warfarin (0.27-0.6)
■ HR of stroke comparing brand dabigatran to warfarin (0.6-0.98)
■ RR of ICH comparing brand aspirin to warfarin (0.16-1.6)
■ HR of MI comparing dabigatran to warfarin (0.89-1.91)
■ Baseline rate of MI on warfarin (0.0093-0.0131)
■ RR of stroke comparing aspirin to warfarin (1.59-2.7)
■ RR of MI comparing aspirin to warfarin (0.84-2.39)
■ HR of ECH comparing brand dabigatran to warfarin (0.78-1.25)
■ Proportion of fatal ECH(0.01-0.04)
■ RR of nonevent death AF and stroke (1.3-3)
■ Proportion of ischemic stroke with no residual deficit with dabigatran (0.091-0.133)
■ Proportion of fatal ICH with dabigatran or aspirin (0.283-0.452)
■ RR of ECH comparing aspirin to warfarin (0.47-2.73)
■ Proportion of fatal MI (0.158-0.174)
■ Proportion of major ICH with dabigatran or aspirin (0.09-0.214)
■ Proportion of minor ischemic stroke with dabigatran (0.348-0.425)
■ Proportion of fatal ischemic stroke with aspirin (0.101-0.179)
■ Proportion of ischemic stroke with no residual deficit with aspirin (0.11-0.133)
■ Proportion of major stroke with aspirin (0.3-0.411)
■ Proportion of fatal stroke with dabigatran (0.082-0.101)
■ Proportion of minor stroke with aspirin (0.348-0.41)
■ Proportion of major stroke with dabigatran (0.402-0.417)
■ RR of minor bleed comparing aspirin to warfarin (0.32-1.22)
■ HR of minor bleed comparing dabigatran to warfarin (0.85-0.97)

A)

Tornado Diagram – Net Monetary Benefit
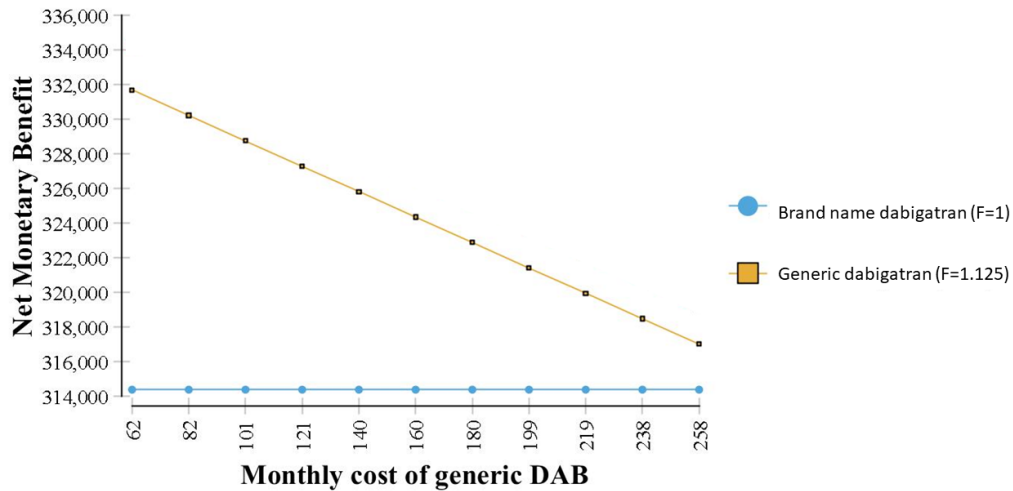## (WTP=100,000)

EV: 687842

NMB

- RR of nonevent death with nonvalvular AF (1.12-1.61)
- HR of ICH comparing brand dabigatran to warfarin (0.27-0.6)
- HR of stroke comparing brand dabigatran to warfarin (0.6-0.98)
- RR of ICH comparing brand aspirin to warfarin (0.16-1.6)
- HR of MI comparing dabigatran to warfarin (0.89-1.91)
- Baseline rate of MI on warfarin (0.0093-0.0131)
- RR of stroke comparing aspirin to warfarin (1.59-2.7)
- RR of nonevent death AF and stroke (1.3-3)
- HR of ECH comparing brand dabigatran to warfarin (0.78-1.25)
- RR of MI comparing aspirin to warfarin (0.84-2.39)
- Proportion of fatal ECH (0.01-0.04)
- Proportion of ischemic stroke with no residual deficit with dabigatran (0.091-0.133)
- RR of ECH comparing aspirin to warfarin (0.47-2.73)
- Proportion of fatal MI (0.158-0.174)
- Proportion of fatal ICH with dabigatran or aspirin (0.283-0.452)
- Proportion of major ICH with dabigatran or aspirin (0.09-0.214)
- Proportion of minor ischemic stroke with dabigatran (0.348-0.425)
- Proportion of ischemic stroke with no residual deficit with aspirin (0.11-0.133)
- Proportion of major stroke with aspirin (0.3-0.411)
- Proportion of fatal ischemic stroke with aspirin (0.101-0.179)
- Proportion of fatal stroke with dabigatran (0.082-0.101)
- Proportion of minor stroke with aspirin (0.348-0.41)
- Proportion of major stroke with dabigatran (0.402-0.417)
- RR of minor bleed comparing aspirin to warfarin (0.32-1.22)
- HR of minor bleed comparing dabigatran to warfarin (0.85-0.97)

B)

Figure S11. Tornado diagram of net monetary benefit comparing brand and less extreme cases of generic dabigatran at varying transition probabilities A) using willingness-to-pay threshold of 50,000 B) using willingness-to-pay threshold of 100,000.
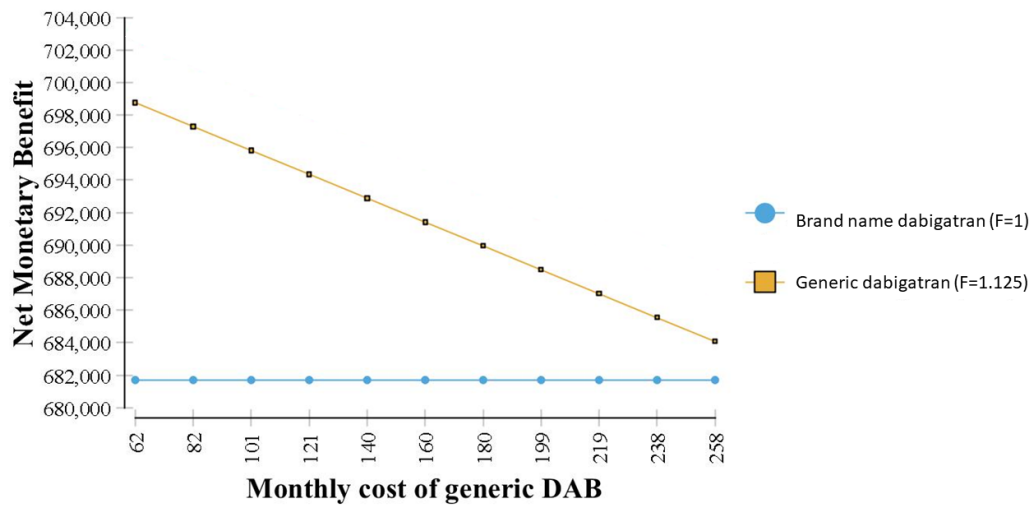
Figure S12-S14 shows the result of one-way sensitivity analysis comparing
brand dabigatran and F=1.125 generic dabigatran.

Sensitivity Analysis (WTP=50,000)

A)

Sensitivity Analysis (WTP=100,000)

B)

Figure S12. Net monetary benefit at varying cost of generic dabigatran comparing
brand dabigatran and F=1.125 generic dabigatran A) using willingness-to-pay
threshold of 50,000 B) using willingness-to-pay threshold of 100,000.

Tornado Diagram – ICER

Monthly cost of ICH (162.22-6036.38)
Monthly cost of major stroke (345.11-2309.36)
Monthly cost of minor stroke (219.05-1461.05)
Event cost of ECH (13300.28-18015.1)
Event cost of ICH (34252.97-61330.89)
Monthly cost of stroke and ICH (206.65-7665.84)
Event cost of MI (30831.8-37906.62)
Event cost of nonevent death (3796.24-8134.95)
Event cost of minor bleed (0-216.99)
Monthly cost of aspirin (0.16-6.42)
Event cost of minor stroke (17453-21816.84)
Monthly cost of MI (551.77-1930.15)
Event cost of RIND (10488.74-13117.39)
Event cost of major stroke (27588.36-34503.02)
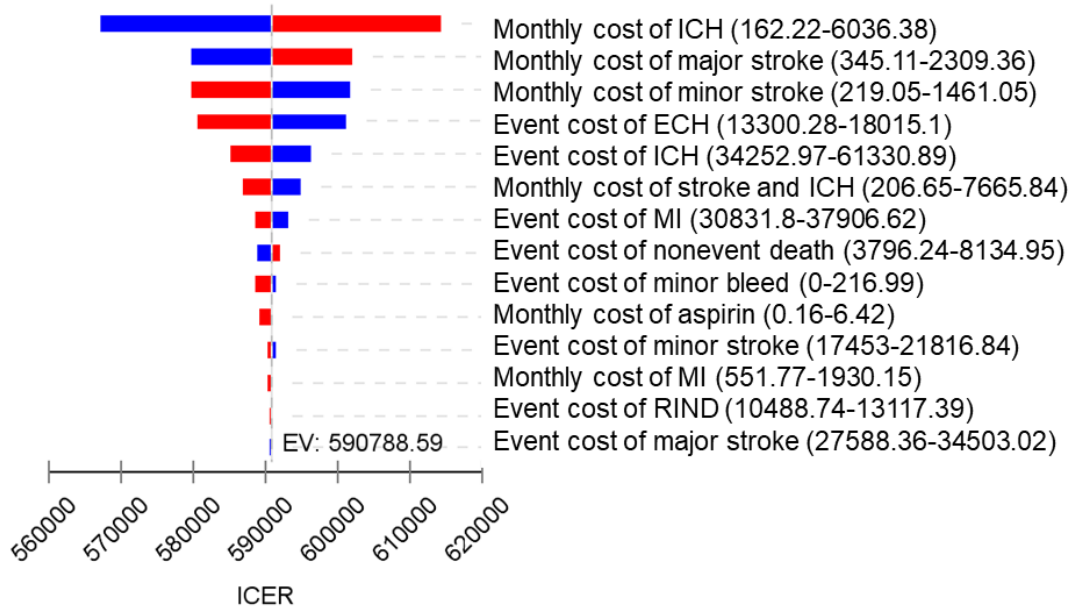
EV: 590788.59

ICER

Figure S13. Tornado diagram of incremental cost-effectiveness ratio at varying event and monthly comparing brand dabigatran and F=1.125 generic dabigatran

Tornado Diagram – ICER

Annual disutility of major neurological event (0-1)
Annual state utility of well with AF on dabigatran (0.975-1)
Annual disutility of minor neurological event (0-1)
Annual state utility of well with AF on aspirin (0.994-1)
Annual disutility of non-ICH bleed event (0-0.3)
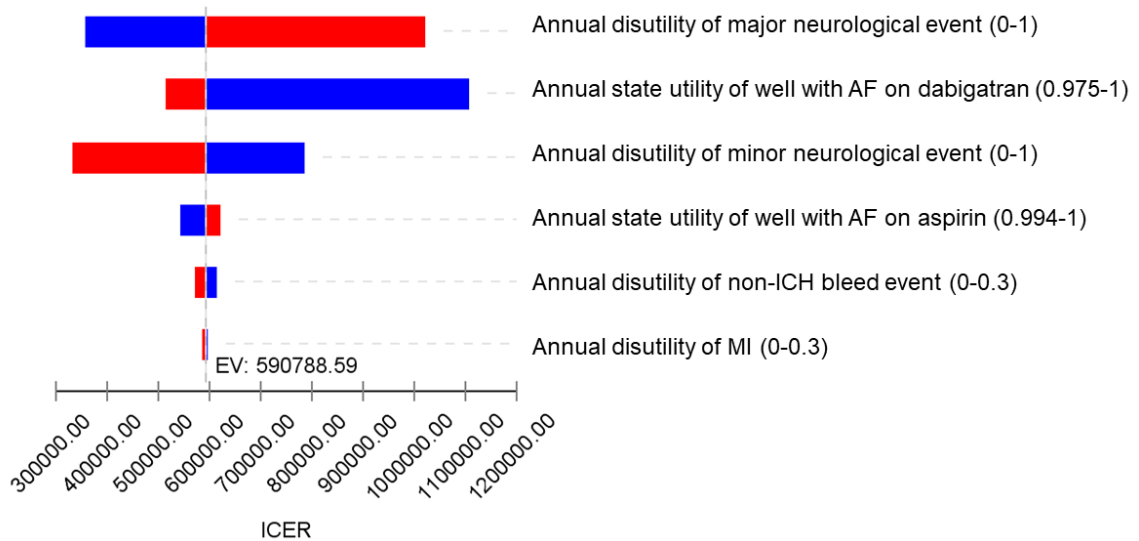Annual disutility of MI (0-0.3)

EV: 590788.59

ICER

Figure S14. Tornado diagram of incremental cost-effectiveness ratio at varying utilities comparing brand dabigatran and F=1.125 generic dabigatran

CE Acceptability Curve Comparing Brand to Generic Dabigatran with extreme systemic exposure
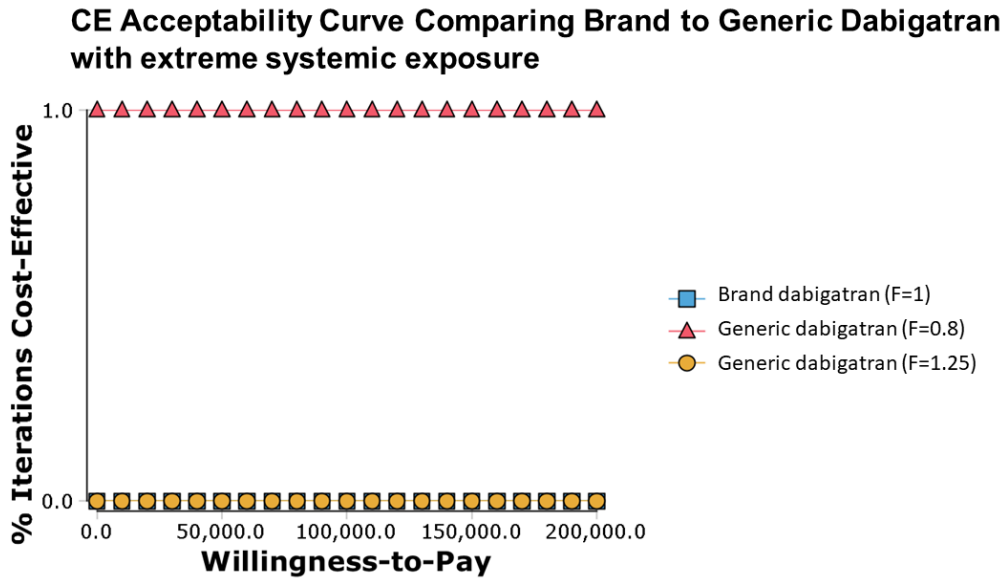
Figure S15. Result of probability sensitivity analysis. Cost-effectiveness (CE) acceptability curve (probability that a treatment will be cost-effective at varying willingness-to-pay thresholds)
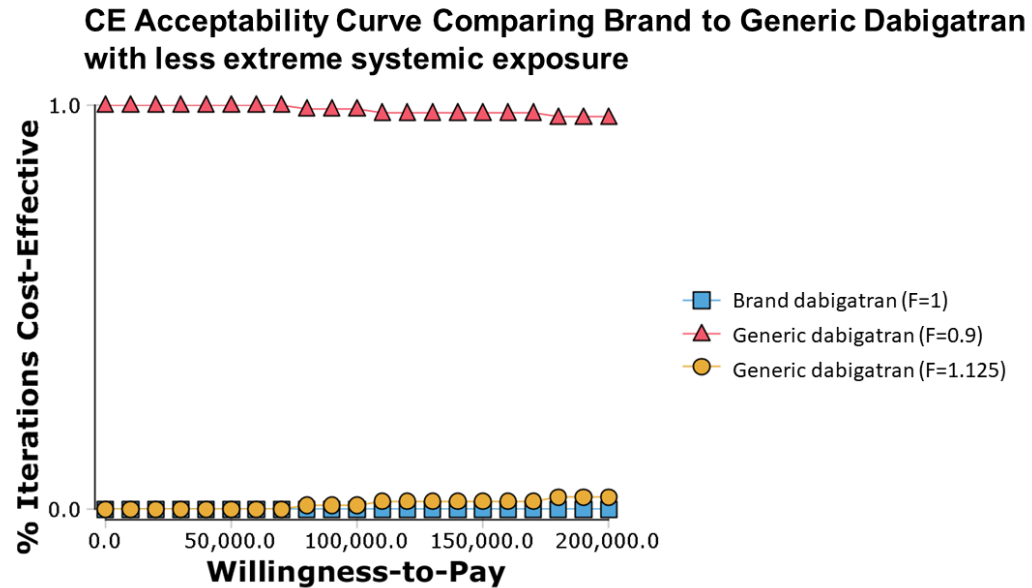

CE Acceptability Curve Comparing Brand to Generic Dabigatran with less extreme systemic exposure

Figure S16. Result of probability sensitivity analysis. Cost-effectiveness (CE) acceptability curve (probability that a treatment will be cost-effective at varying willingness-to-pay thresholds)

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